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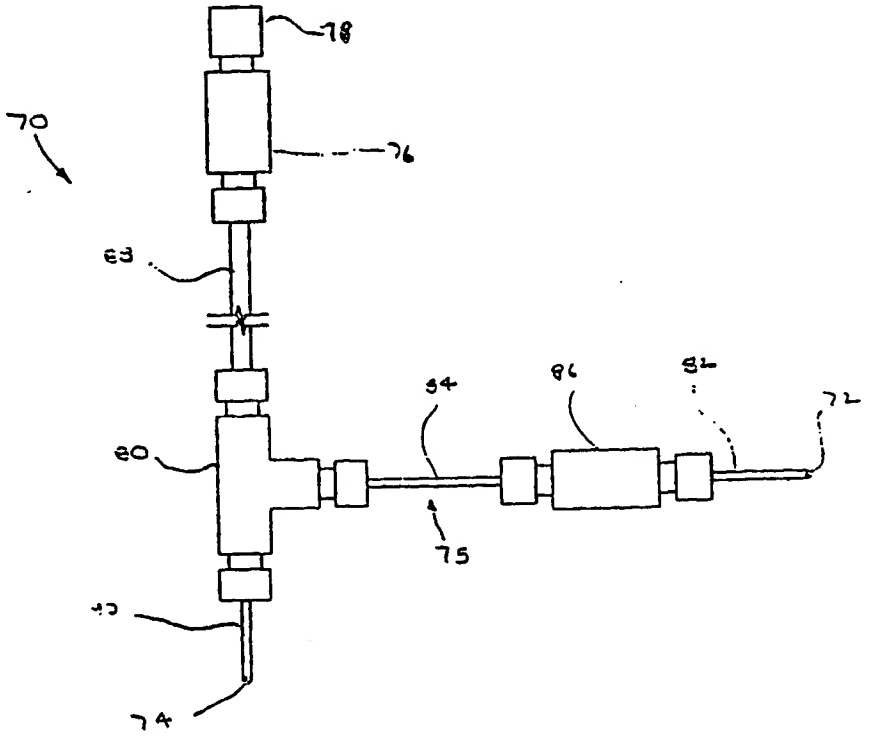
(54) Title: PULSE DAMPER

(57) Abstract

A fluidic driver system for use with a cartridge in a microfluidic analysis instrument. The driver system includes linear pumps, differential pumps, fluidic capacitive filters, and face seal assemblies which act to provide a consistent and smooth fluid flow through the instrument, thus improving the accuracy of the analysis.



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PULSE DAMPER

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates generally to microfluidic devices for performing analytical testing and, in particular, to a fluidic driver system for use with microfluidic cartridges.

2. Description of the Related Art

Microfluidic devices have recently become popular for performing analytical testing. Using tools developed by the semiconductor industry to miniaturize electronics, it has become possible to fabricate intricate fluid systems which can be inexpensively mass produced. Systems have been developed to perform a variety of analytical techniques for the acquisition of information for the medical field.

A process called "field-flow fractionation" (FFF) has been developed to separate and analyze molecules and particles for analysis by the use of a force applied across a flow channel carrying a variety of particle sizes. Examples of this method are taught in U.S. Patent Nos. 3,449,938; 4,147,621; 4,214,981; 4,830,756; and 5,156,039.

A related method for particle fractionation is the "Split Flow Thin Cell" (SPLITT) process. This process has been used to develop devices having mesoscale functional element capable of rapid, automated analyses of preselected molecular or cellular analytes in a range of biological and other applications. Examples of this method are taught in U.S. Patent Nos. 5,296,375; 5,304,487; 5,486,335; and 5,498,392.

Still another method used for assaying fluids involves application of electrical fields to a microfluidic system for providing capillary electrophoresis to separate materials in a flow channel. Examples of this process are taught in U.S. Patent Nos. 5,699,157; 5,779,868; and 5,800,690.

U.S. Patent No. 5,716,852 teaches yet another method for analyzing the presence and concentration of small particles in a flow cell using diffusion principles. This patent, the disclosure of which is incorporated herein by reference, discloses a channel cell system for detecting the presence of analyte particles in a sample stream using a laminar flow channel having at least two inlet means which provide an indicator stream and a sample stream, where the laminar flow channel has a depth sufficiently small to allow laminar flow of the streams and length sufficient to allow diffusion of particles of the analyte into the indicator stream to form a detection area, and having an outlet out of the channel to form a single mixed stream. This device, which is known as a T-Sensor, contains an external detecting means for detecting changes in the indicator stream. This detecting means may be provided by

any means known in the art, including optical means such as optical spectroscopy, or absorption spectroscopy or fluorescence.

A sample microfluidic analysis instrument for performing analytical testing which uses a disposable fluidic analysis cartridge is disclosed in U.S. Patent Application Serial No. 09/080,691, which was filed on May 18, 1998, the disclosure of which is incorporated herein by reference. This instrument includes a cartridge holder, a flow cytometric measuring apparatus positioned for optical coupling with a flow cytometric measuring region on the cartridge, and a second measuring apparatus positioned to be coupled with a second analysis region on the cartridge. The cartridge holder includes alignment markings to mate with cartridge alignment markings. It also includes pump mechanisms to coupled with pump interfaces on the cartridges and valve mechanisms to couple with valve interfaces on the cartridge.

In this type of system, valve and pump mechanisms are external to the cartridge, while the cartridge includes the valve and pump interfaces. Upon loading the cartridge into the apparatus, the valve and pump mechanisms engage the valve and pump interfaces. Thus, it is critical that the interfaces provide an efficient and precise coupling between the cartridge and the external mechanisms. In addition, it is imperative that these external devices provide for a smooth flow of the fluids into and out of the cartridge to ensure accurate measurements within a microfluidic analysis system.

SUMMARY OF THE INVENTION

It is therefore an object of the present invention to provide an efficient interface between the cartridge and the external pumps and valves of a microfluidic analysis system.

It is a further object of the present invention to provide pumping systems for using a microfluidic assembly which produce a consistently smooth and even fluid flow through the system for accurate analysis.

These and other objects of the present invention will be more readily apparent in the description that follows.

BRIEF DESCRIPTON OF THE DRAWINGS

FIG. 1 is an exploded view of a linear pump for use in the present invention;

FIG. 2 is a side elevational view of the pump of FIG. 1;

FIG. 3 is an end view of the pump of FIG. 1;

FIG. 4 is a top elevational view of the differential pump system of the present invention;

FIG. 5 is an end view of the differential pump of FIG. 4;

FIG. 6 is a plan view of the fluidic capacitor assembly of the present invention; and

FIG. 7 is a cross-sectional view of the face seal assembly of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Referring more particularly to the drawings, there is shown in FIGS. 1-3 a linear pump assembly, generally indicated at 10, which embodies the principles of the present invention. Pump 10 consists of a linear stepper motor unit 12, a mounting bracket 14, an optical switch 16, a precision bore glass syringe 18, a zero dead volume manifold 20, and a valve 22. Also included is a plurality of screws 24 for attaching manifold 20 to bracket 14, a pair of screws 26 and clinch nuts 28 for mounting switch 16 within bracket 14, and a pair of screws 30 and clinch nuts 32 for mounting motor unit 12 to bracket 14. As can be clearly seen in FIG. 2, motor 12, syringe 18, and manifold 20 are arranged in a linear configuration to minimize off-axis torque. Manifold 20 contains a cross channel 34 which connects to valve 22 and to fittings for connection to external fluid components (not shown). To reduce the hold up volume to near zero dead volume, the piston of syringe 18 intrudes into cross channel 34 at the end of its delivery stroke. Valve 22 is embedded within manifold 20 with short interconnections for the input and output of pump assembly 10.

In operation, linear stepper motor assembly 10 converts rotational movement to linear displacement via motor unit 12 coupled to syringe 18. Motor unit 12 offers movement per step of .001 inch and .00025 inch with a total stroke length of .520 inches. The bores of syringe 18 can range from .028 to .583 inches in diameter. By combining these components in different arrangements, a total volume displacement can range from 5 microliters to 4 milliliters.

Stepper motor unit 12 is controlled using a microstepper controller (not shown) which further portitions each full step to as much as 256 microsteps. Thus, accurate and smooth position resolution can be achieved at the microstep level, and flow rates can be as low as 1/256 of the full step rate. Flow rates using pump assembly 12 range from .0025 microliter/step to 4.314 microliter/step with a consistent and smooth flow rate to insure accuracy.

In practice, it is difficult to reliably achieve a smooth and constant fluid flow in microfluidic systems, due to stiction in the sliding piston of the syringe, and also as a result of elasticity in the drive components of the system. To avoid these obstacles for very small volume displacements, two pumps are connected to a common cross channel.

FIGS. 4 and 5 illustrate an alternative embodiment of the present invention which employs a differential pump system. Referring now to FIG. 4, a differential pump system, generally designated at 50, includes a mounting bracket 52, a pair of linear stepper motor units 54a and 54b, a pair of glass syringes 56a and 56b corresponding to motor units 54a and 54b, a pair of optical switches 58a and 58b

corresponding to motor units 54a and 54b, and a manifold 60 having a cross channel 62. Syringes 56a and 56b are coupled to motor units 54a and 54b to translate rotary motion into linear motion.

Pumps 54a and 54b are driven differentially, with one advancing while the other is receding. In this manner, the net output from cross channel 62 will be the difference in the velocities of the two pumps. Thus, the velocities and displacements of the individual pumps are located within a range above the conditions where elasticity and stiction are a major component of the volume displacement, whereby providing a constant and smooth fluid flow within the system to increase the accuracy of the analysis performed by the system.

Another device which is helpful in reducing fluctuation in the fluid flow of the microfluidic analysis system is shown in FIG. 6. Referring now to FIG. 6, there is shown a fluidic filter assembly, generally designated at 70. Assembly 70 includes an input port 72, an output port 74, a restrictor section 75, an accumulator section 76 which terminates in an end cap 78, and a T-connector 80 which couples input port 72 to accumulator 76. Assembly 70 acts as a fluidic filter which reduces any fluid pulses that are introduced into the fluid discharge by stiction and/or stepper motor cogging.

Input port 72 includes a section of tubing 82 which is preferably constructed from .04 inch internal diameter (ID) tubing in the present embodiment. Tubing 82 is coupled to restrictor section 75, which consists of a section of smaller tubing 84, by a connector 86. Tubing 84 consists of a section of .005 inch ID tubing that is at least 1 inch long, and is coupled at its opposite end to T-connector 80. Accumulator section 76 is constructed from a section of tubing 88 which has an ID of .06 inches in the present embodiment, and is 8 inches long. Tubing 88 couples T-connector 80 to accumulator section 76. Output port 74 is coupled to T-connector 80 by a section of tubing 90 having an ID of .04 inches.

In operation, fluid enters input port 72 via tubing 82 and passes through T-connector 80 which includes the accumulator section 76 which then connects to tubing 84, which acts as a flow restrictor, as it has a smaller ID. This assembly configuration acts as a filter to reduce any pulsing discharge to an acceptable smooth and continuous flow level. The fluid flow then exits port 74 via tubing 90 which is the same size as the input line. By using assembly 70, the operation of the microfluidic device can be significantly improved. During operation of this configuration, as a fluid is driven into the input port 72, passing through tubing 82 and coupling 86, it further passes through restrictor 75, developing a pressure drop across restrictor 75. This pressure will be equilibrated by a rise in fluid in accumulator 76 until the trapped volume of air is compressed to the extent required to equalize the pressure drop across restrictor 75. This configuration will exhibit a time constant dependent upon the trapped volume in accumulator 76 and the restrictivity of restrictor 75. Looking forward into the input port 70, any pulsation in the flow will be absorbed by accumulator 76. Looking backwards into exit port 74, such pressure pulses will discharge slowly according to the time constant of filter system 70.

Another device for improving the operation of a microfluidic analysis system is shown in FIG. 7. A face seal assembly, generally designated at 100, consists of a thin flexible elastomeric gasket 102 which is located within a fluidic analysis cartridge 104 as taught in Serial No. 09/808,191. Gasket 102 is located between a top plate 106 and a bottom plate 108 of cartridge 104, and is held in position by a laminate section 110. A ring-shaped surface 112 of gasket 102 is positioned between the lower surface 102a of gasket 102 and the upper surface 110a of laminate section 110 opposite a port 114 within cartridge 104. When cartridge 104 is properly positioned within the analysis device, a locating surface 116 of the device mates within an aperture 118 of cartridge 104 to ensure proper orientation. In this position, an extension 120 from a manifold 122 of the device is forced against gasket 102, causing a face seal between the two parts, and thus allowing fluid discharge from extension 120 to enter cartridge 104 in a smooth and efficient manner. Gasket 102 is constructed such that is provides a force against the bottom surface of extension 120, guaranteeing an adequate sealing force between the surfaces. Multiple face seals are employed within cartridge 104 to provide for multiple reagent and/or sample inputs. In addition, extension 120, which in the present embodiment is a tubular structure having an internal passageway 124, interacts with flexible gasket 102 to provide a spring loading effect which acts to hold the bottom surface of extension 120 tightly against gasket 102.

While the present invention has been shown and described in terms of the preferred embodiments thereof, it will be understood that this invention is not limited to this particular embodiment and that many changes of modifications may be made without departing from the true spirit and scope of the invention as defined in the appended claims.

What is claimed is:

1. A fluidic filter assembly for reducing fluctuations in fluid flow within microfluidic channels, comprising:

inlet means;

outlet means;

an accumulator section;

and means for coupling said inlet means, said outlet means, and said accumulator section,

whereby fluctuation in fluid flowing into said inlet means are reduced by said accumulator section before said fluid exits said outlet means.

2. The assembly of claim 1, wherein said inlet and outlet means comprise tubing having an internal diameter of 0.040 inches.

3. The assembly of claim 1, wherein said coupling means comprises a T-connector.

4. The assembly of claim 1, further comprising a restrictor, located between said inlet means and said coupling means, having an internal diameter less than that of said inlet means.

5. The assembly of claim 4, wherein said restrictor has an internal diameter of 0.005 inches.

6. The assembly of claim 1, wherein said accumulator includes tubing having an internal diameter of 0.06 inches.

7. The assembly of claim 6, wherein said tubing measures approximately 8 inches in length.

8. The assembly of claim 1, wherein said accumulator section includes an end cap at its end opposite said coupling means.

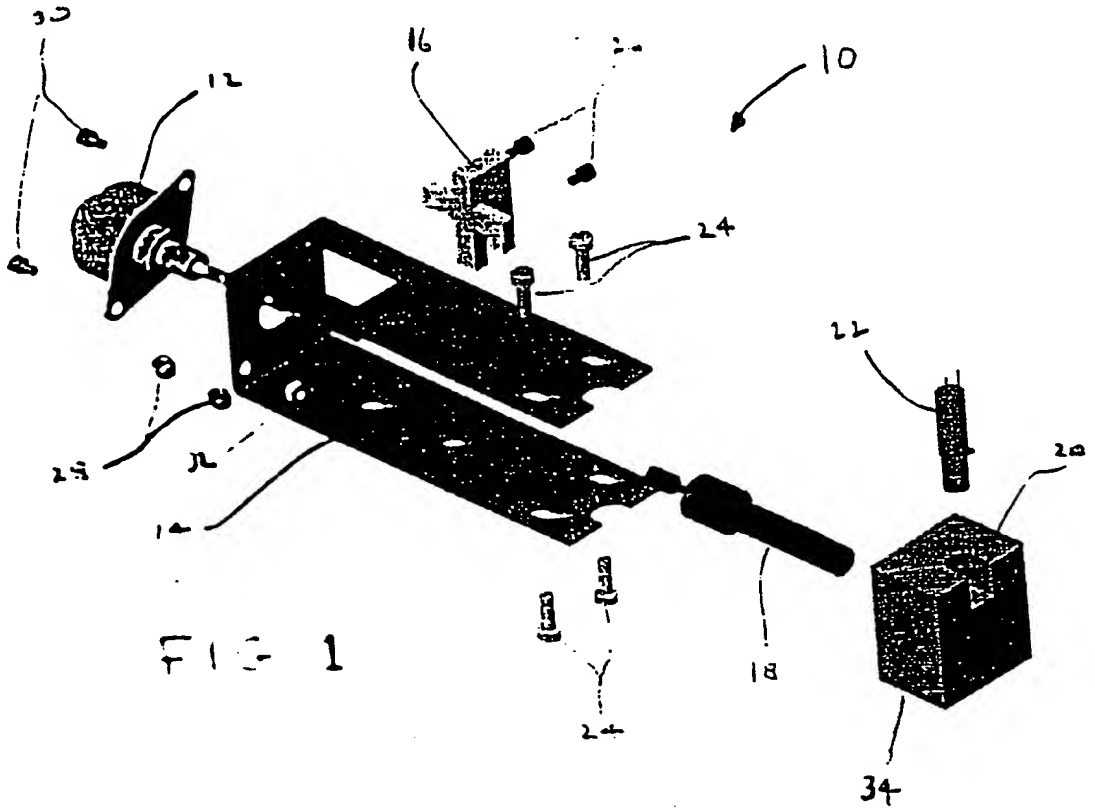

FIG. 1

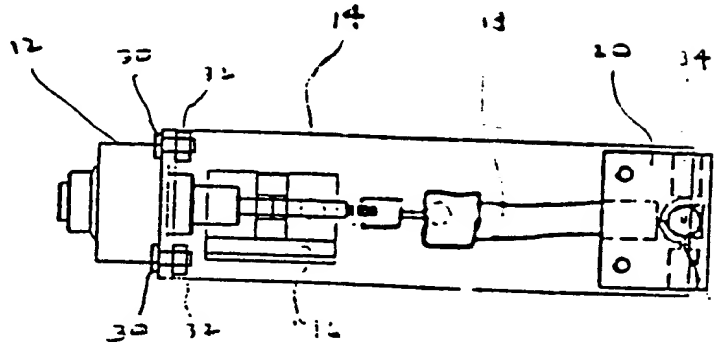

FIG. 2

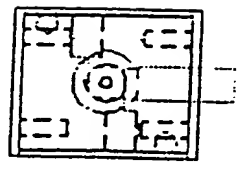

FIG. 3

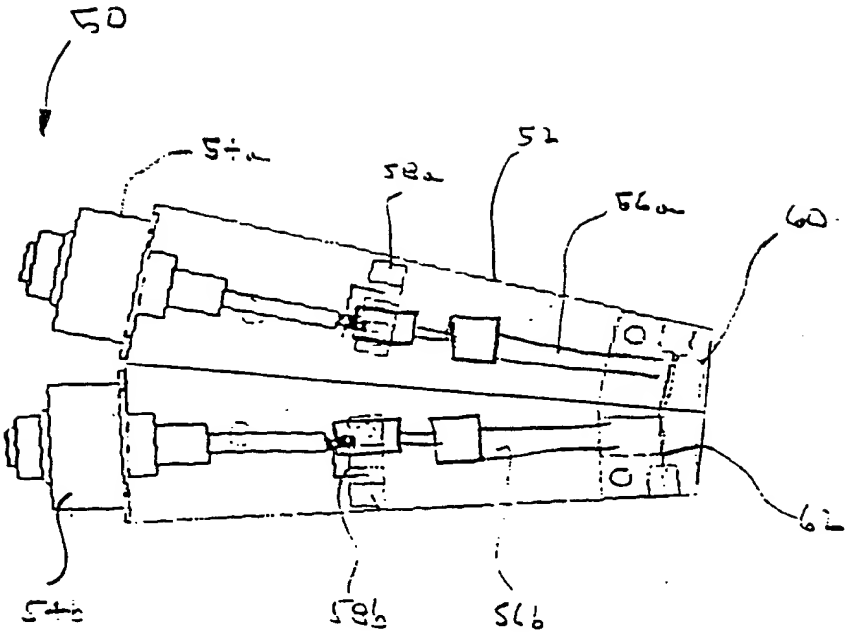

FIG. 4

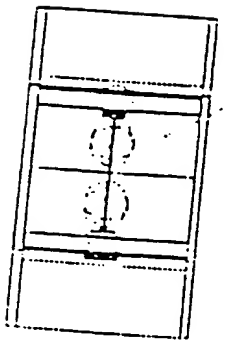

FIG. 5

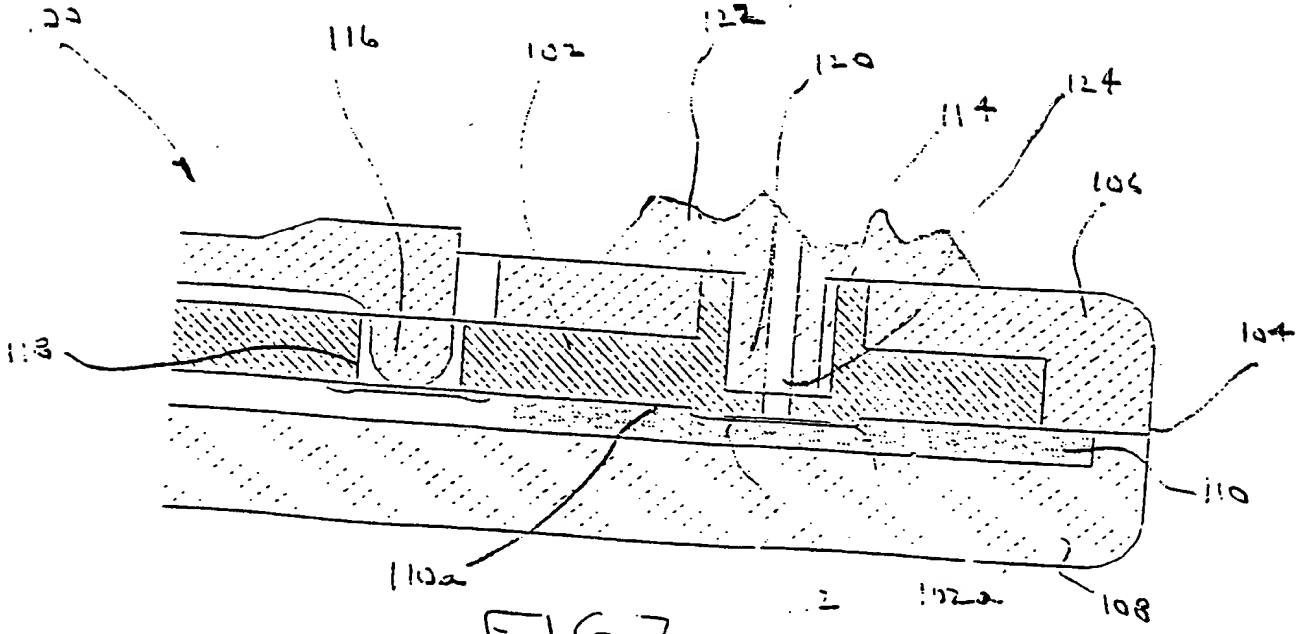

FIG. 7

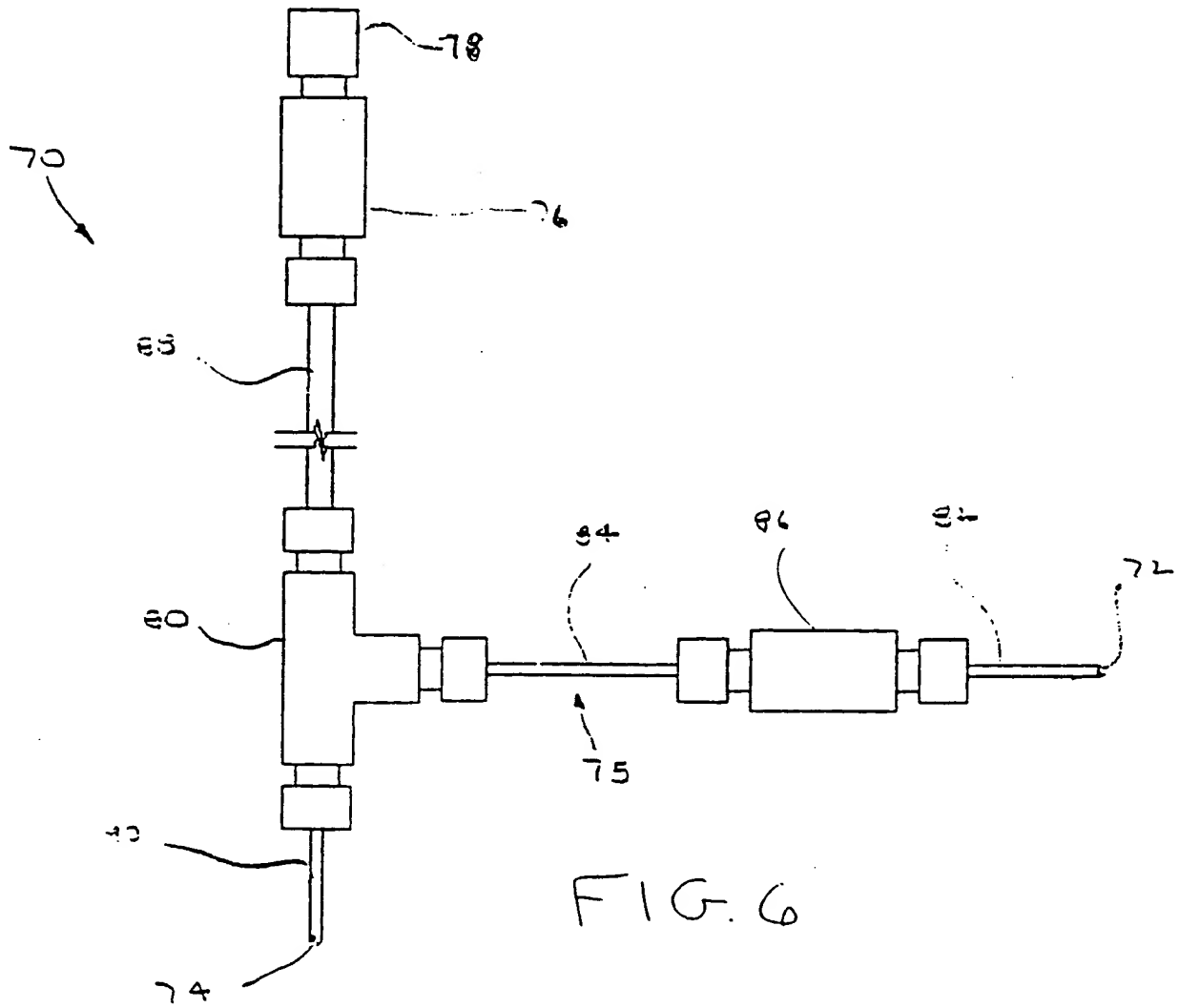

FIG. 6

INTERNATIONAL SEARCH REPORT

Int ional Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N30/32 F04B11/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N F04B B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 024 061 A (GATISS JOHN WILLIAM) 17 May 1977 (1977-05-17)	1-3
A	column 4, line 47 -column 6, line 29 column 7, line 22-40 column 7, line 67 -column 8, line 28	4
X	US 4 629 562 A (KERCHER PAUL W) 16 December 1986 (1986-12-16) column 2, line 65 -column 3, line 26	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
21 June 2000	28/06/2000

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

information on patent family members

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PCT/US 00/06809

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4024061 A	17-05-1977	GB 1464024 A	09-02-1977
		DE 2540060 A	25-03-1976
US 4629562 A	16-12-1986	NONE	

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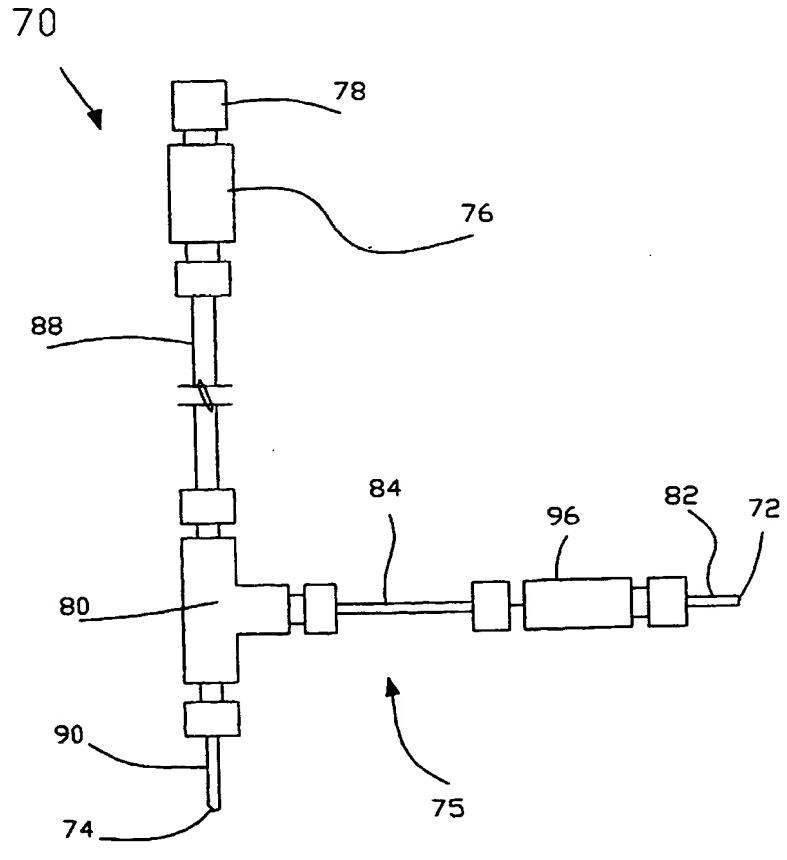

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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BACKGROUND OF THE INVENTION

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DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Referring more particularly to the drawings, there is shown in FIGS. 1-3 a linear pump assembly, generally indicated at 10, which embodies the principles of the present invention. Pump 10 consists of a linear stepper motor unit 12, a mounting bracket 14, an optical switch 16, a precision bore glass syringe 18, a zero dead volume manifold 20, and a valve 22. Also included is a plurality of screws 24 for attaching manifold 20 to bracket 14, a pair of screws 26 and clinch nuts 28 for mounting switch 16 within bracket 14, and a pair of screws 30 and clinch nuts 32 for mounting motor unit 12 to bracket 14. As can be clearly seen in FIG. 2, motor 12, syringe 18, and manifold 20 are arranged in a linear configuration to minimize off-axis torque. Manifold 20 contains a cross channel 34 which connects to valve 22 and to fittings for connection to external fluid components (not shown). To reduce the hold up volume to near zero dead volume, the piston of syringe 18 intrudes into cross channel 34 at the end of its delivery stroke. Valve 22 is embedded within manifold 20 with short interconnections for the input and output of pump assembly 10.

In operation, linear stepper motor assembly 10 converts rotational movement to linear displacement via motor unit 12 coupled to syringe 18. Motor unit 12 offers movement per step of .001 inch and .00025 inch with a total stroke length of .520 inches. The bores of syringe 18 can range from .028 to .583 inches in diameter. By

combining these components in different arrangements, a total volume displacement can range from 5 microliters to 4 milliliters.

Stepper motor unit 12 is controlled using a microstepper controller (not shown) which further portitions each full step to as much as 256 microsteps. Thus, accurate and smooth position resolution can be achieved at the microstep level, and flow rates can be as low as 1/256 of the full step rate. Flow rates using pump assembly 12 range from .0025 microliter/step to 4.314 microliter/step with a consistent and smooth flow rate to insure accuracy.

In practice, it is difficult to reliably achieve a smooth and constant fluid flow in microfluidic systems, due to stiction in the sliding piston of the syringe, and also as a result of elasticity in the drive components of the system. To avoid these obstacles for very small volume displacements, two pumps are connected to a common cross channel.

FIGS. 4 and 5 illustrate an alternative embodiment of the present invention which employs a differential pump system. Referring now to FIG. 4, a differential pump system, generally designated at 50, includes a mounting bracket 52, a pair of linear stepper motor units 54a and 54b, a pair of glass syringes 56a and 56b corresponding to motor units 54a and 54b, a pair of optical switches 58a and 58b corresponding to motor units 54a and 54b, and a manifold 60 having a cross channel 62. Syringes 56a and 56b are coupled to motor units 54a and 54b to translate rotary motion into linear motion.

Pumps 54a and 54b are driven differentially, with one advancing while the other is receding. In this manner, the net output from cross channel 62 will be the difference in the velocities of the two pumps. Thus, the velocities and displacements of the individual pumps are located within a range above the conditions where elasticity and stiction are a major component of the volume displacement, whereby providing a constant and smooth fluid flow within the system to increase the accuracy of the analysis performed by the system.

Another device which is helpful in reducing fluctuation in the fluid flow of the microfluidic analysis system is shown in FIG. 6. Referring now to FIG. 6, there is shown a fluidic filter assembly, generally designated at 70. Assembly 70 includes an input port 72, an output port 74, a restrictor section 75, an accumulator section 76 which terminates in an end cap 78, and a T-connector 80 which couples input port 72 to accumulator 76. Assembly 70 acts as a fluidic filter which reduces any fluid pulses that are introduced into the fluid discharge by stiction and/or stepper motor cogging.

Input port 72 includes a section of tubing 82 which is preferably constructed from .04 inch internal diameter (ID) tubing in the present embodiment. Tubing 82 is coupled to restrictor section 75, which consists of a section of smaller tubing 84, by a connector 86. Tubing 84 consists of a section of .005 inch ID tubing that is at least 1 inch long, and is coupled at its opposite end to T-connector 80. Accumulator section 76 is constructed from a section of tubing 88 which has an ID of .06 inches in the present embodiment, and is 8 inches long. Tubing 88 couples T-connector 80 to

accumulator section 76. Output port 74 is coupled to T-connector 80 by a section of tubing 90 having an ID of .04 inches.

In operation, fluid enters input port 72 via tubing 82 and passes through T-connector 80 which includes the accumulator section 76 which then connects to tubing 84, which acts as a flow restrictor, as it has a smaller ID. This assembly configuration acts as a filter to reduce any pulsing discharge to an acceptable smooth and continuous flow level. The fluid flow then exits port 74 via tubing 90 which is the same size as the input line. By using assembly 70, the operation of the microfluidic device can be significantly improved. During operation of this configuration, as a fluid is driven into the input port 72, passing through tubing 82 and coupling 86, it further passes through restrictor 75, developing a pressure drop across restrictor 75. This pressure will be equilibrated by a rise in fluid in accumulator 76 until the trapped volume of air is compressed to the extent required to equalize the pressure drop across restrictor 75. This configuration will exhibit a time constant dependent upon the trapped volume in accumulator 76 and the restrictivity of restrictor 75. Looking forward into the input port 70, any pulsation in the flow will be absorbed by accumulator 76. Looking backwards into exit port 74, such pressure pulses will discharge slowly according to the time constant of filter system 70.

Another device for improving the operation of a microfluidic analysis system is shown in FIG. 7. A face seal assembly, generally designated at 100, consists of a thin flexible elastomeric gasket 102 which is located within a fluidic analysis cartridge 104 as taught in Serial No. 09/808,191. Gasket 102 is located between a top plate

106 and a bottom plate 108 of cartridge 104, and is held in position by a laminate section 110. A ring-shaped surface 112 of gasket 102 is positioned between the lower surface 102a of gasket 102 and the upper surface 110a of laminate section 110 opposite a port 114 within cartridge 104. When cartridge 104 is properly positioned within the analysis device, a locating surface 116 of the device mates within an aperture 118 of cartridge 104 to ensure proper orientation. In this position, an extension 120 from a manifold 122 of the device is forced against gasket 102, causing a face seal between the two parts, and thus allowing fluid discharge from extension 120 to enter cartridge 104 in a smooth and efficient manner. Gasket 102 is constructed such that is provides a force against the bottom surface of extension 120, guaranteeing an adequate sealing force between the surfaces. Multiple face seals are employed within cartridge 104 to provide for multiple reagent and/or sample inputs. In addition, extension 120, which in the present embodiment is a tubular structure having an internal passageway 124, interacts with flexible gasket 102 to provide a spring loading effect which acts to hold the bottom surface of extension 120 tightly against gasket 102.

While the present invention has been shown and described in terms of the preferred embodiments thereof, it will be understood that this invention is not limited to this particular embodiment and that many changes of modifications may be made without departing from the true spirit and scope of the invention as defined in the appended claims.

What is claimed is:

1. A fluidic filter assembly for reducing fluctuations in fluid flow within microfluidic channels, comprising:

inlet means;

outlet means;

an accumulator section;

and means for coupling said inlet means, said outlet means, and said accumulator section,

whereby fluctuation in fluid flowing into said inlet means are reduced by said accumulator section before said fluid exits said outlet means.

2. The assembly of claim 1, wherein said inlet and outlet means comprise tubing having an internal diameter of 0.040 inches.

3. The assembly of claim 1, wherein said coupling means comprises a T-connector.

4. The assembly of claim 1, further comprising a restrictor, located between said inlet means and said coupling means, having an internal diameter less than that of said inlet means.

5. The assembly of claim 4, wherein said restrictor has an internal diameter of 0.005 inches.

6. The assembly of claim 1, wherein said accumulator includes tubing having an internal diameter of 0.06 inches.

7. The assembly of claim 6, wherein said tubing measures approximately 8 inches in length.

8. The assembly of claim 1, wherein said accumulator section includes an end cap at its end opposite said coupling means.

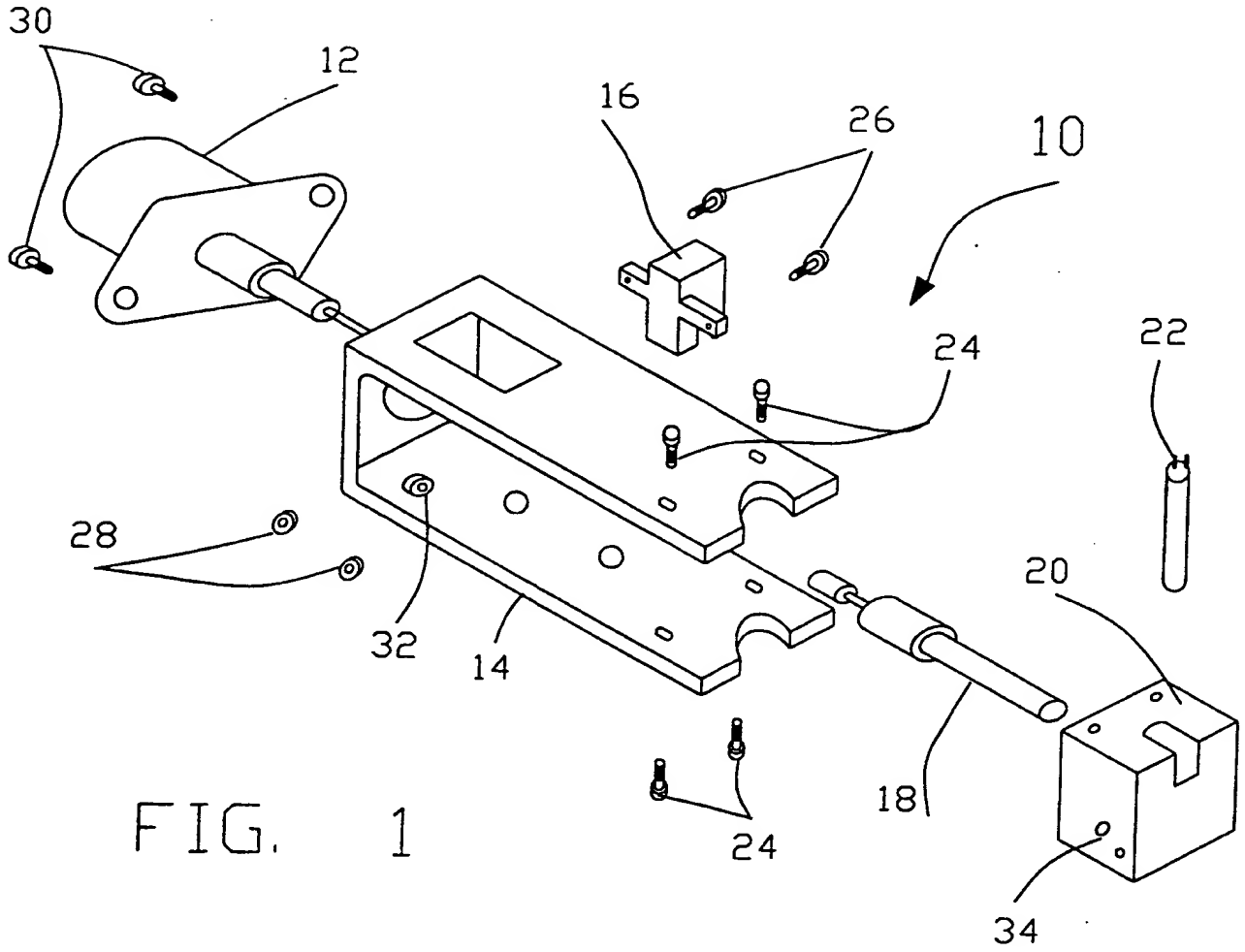

FIG. 1

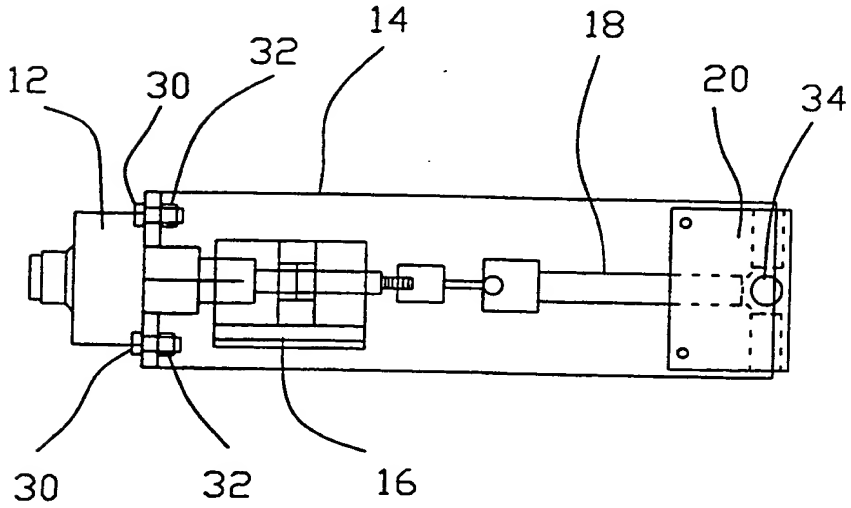

FIG. 2

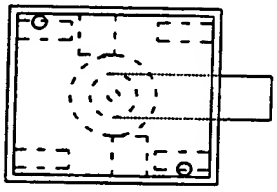

FIG. 3

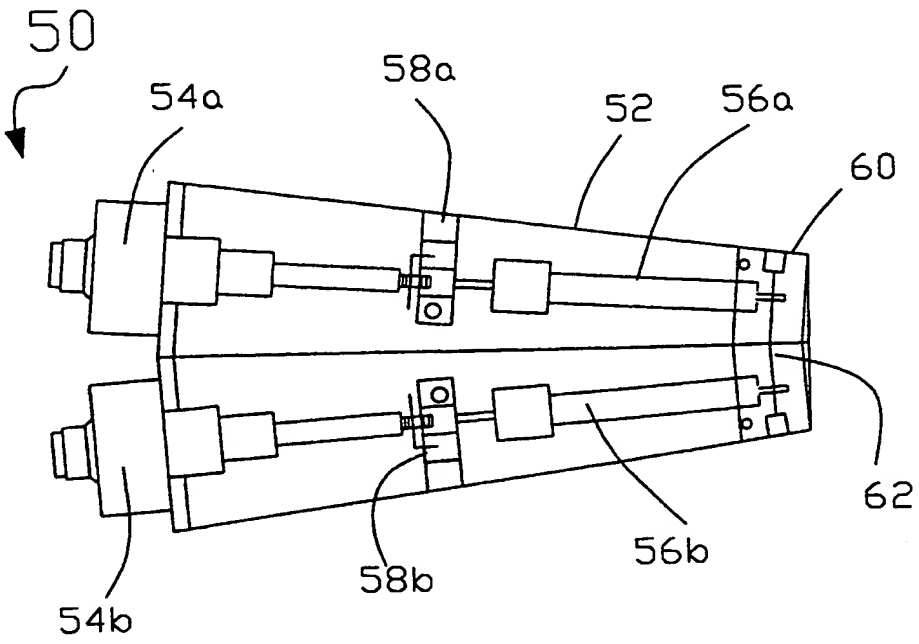

FIG. 4

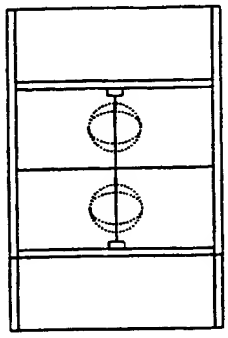

FIG. 5

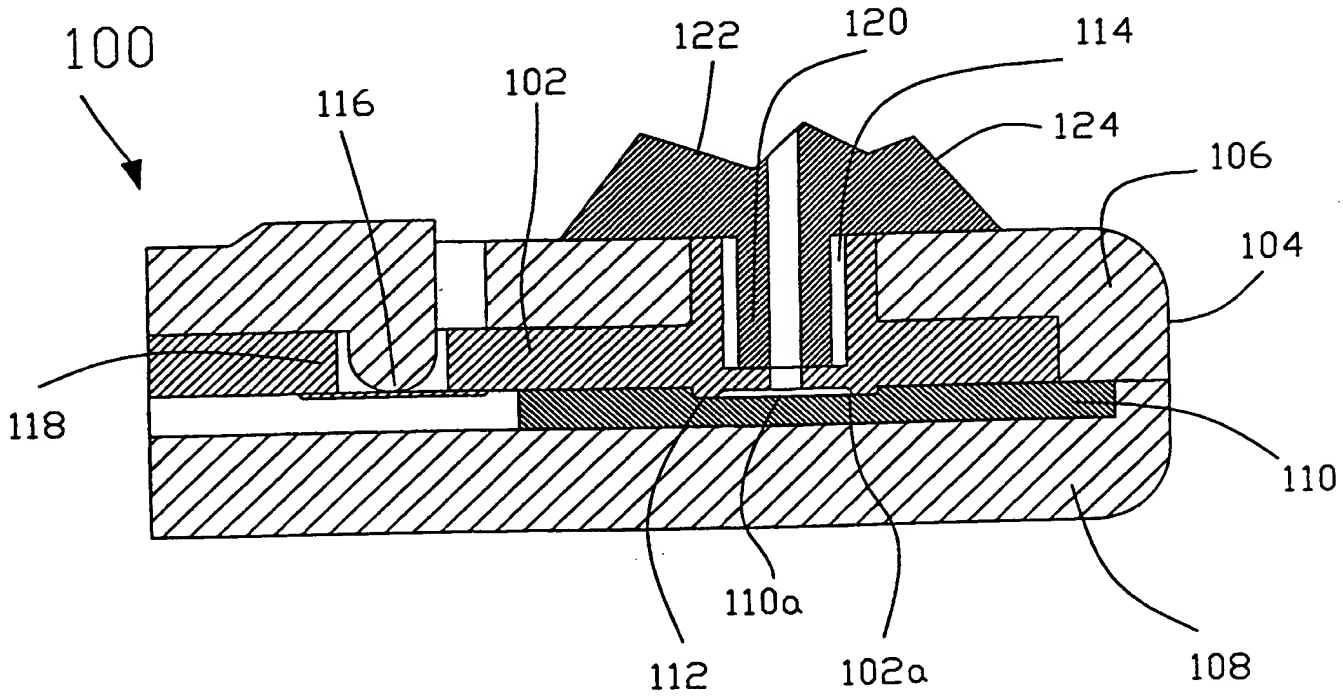

FIG. 7

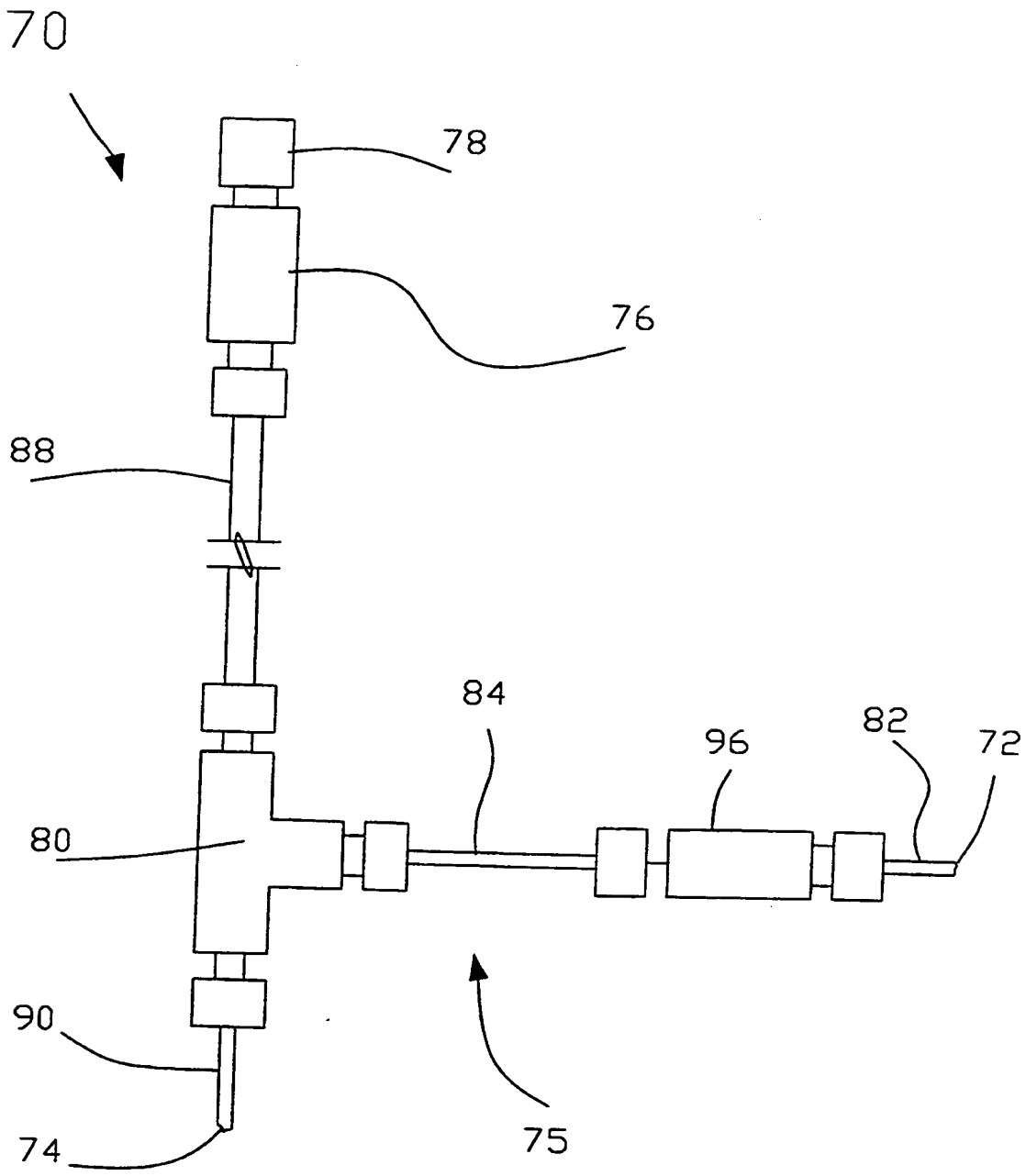

FIG. 6

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 00/06809

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N30/32 F04B11/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N F04B B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 024 061 A (GATISS JOHN WILLIAM) 17 May 1977 (1977-05-17)	1-3
A	column 4, line 47 -column 6, line 29 column 7, line 22-40 column 7, line 67 -column 8, line 28	4
X	US 4 629 562 A (KERCHER PAUL W) 16 December 1986 (1986-12-16) column 2, line 65 -column 3, line 26	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 June 2000	28/06/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Zinngrebe, U

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

information on patent family members

Inte onal Application No
PCT/US 00/06809

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4024061 A	17-05-1977	GB 1464024 A	09-02-1977
		DE 2540060 A	25-03-1976
US 4629562 A	16-12-1986	NONE	